Amendments to the Title:

Please replace the Title with the following amended Title:

~~METHOD OF DETECTING GENETIC POLYMORPHISM~~ OLIGONUCLEOTIDES HAVING A 2'-0,4'-C-ETHYLENE NUCLEOTIDE IN THE THIRD POSITION OF THE 3'-END

Amendments to the Specification:

Please replace the paragraph bridging pages 17 and 18 with the following amended paragraph:

Figure 1 shows the situation when there is no mutation (polymorphism) in a nucleic acid sequence. (i) is a template nucleic acid of a target in which it is intended to examine mutation (polymorphism) in the nucleic acid sequence, and it has the sequence 3'-ATGC-5' as a nucleotide sequence portion thereof. This template nucleic acid is annealed with oligonucleotide [[(ii)in]] (ii) in which the third position from the 3'-end thereof has been modified with ENA (a 2'-*O*,4'-*C*-ethylene-5-methyluridine unit is represented by eT), so as to form a double strand. In this case, at least the 3'-end of the nucleotide sequence of (ii) has a structure that is complementary to the corresponding base, and (ii) and (i) form a double strand. The 3'-end portion of oligonucleotide (ii) forming such a double strand is recognized by nucleic acid synthesizing enzyme (iii), and the nucleic acid synthesis reaction is continued. Specific nucleotide sequences shown in the figure are used for explanation, and thus, it does not mean that the present invention is effective only for such nucleotide sequences.

Please replace the paragraph bridging pages 64 and 65 with the following amended paragraph:

(Example 1)

Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^p-$5C^{e2p}$-T^p-C^t (SEQ ID NO: 11)

Using an automated nucleic acid synthesizer (ABI model 394 DNA/RNA synthesizer, manufactured by Perkin Elmer), the program was carried out at a scale of 40 nmol. With regard to the concentrations of a solvent, reagent and phosphoramidite in each synthesis cycle, the same concentrations as those for synthesis of a natural oligonucleotide were applied. Approximately 0.1 μmol of CPG was used. As a non-natural phosphoramidite, the compound described in Example 22 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene 4-N-benzoyl-5-methylcytidine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. A protected oligonucleotide analogue having a sequence of interest was treated with concentrated ammonia water, so as to separate the oligomer from the support and to remove a cyanoethyl group as a protecting group on a phosphorus atom and a protecting group on a nucleobase. The solvent was evaporated under reduced pressure and the residue was purified by reverse phase HPLC (LC-10VP manufactured by Shimadzu Corporation, column: Merck, ~~Chromolith~~ CHROMOLITH® Performance RP-18e (4.6 × 100 mm) (a HPLC column containing a single rod of high purity monolithic

silica), solution A: 5% acetonitrile, 0.1 M triethylamine acetate aqueous solution (TEAA), pH 7.0; solution B: acetonitrile, B%: 10% → 50% (10 min, linear gradient); 60°C; 2 ml/min; 254 nm), so as to collect the peak of a product of interest having a dimethoxytrityl group. Thereafter, water was added thereto, and the mixture was then concentrated under reduced pressure, so as to remove TEAA. Thereafter, an 80% acetic acid aqueous solution (200 µl) was added and the mixture was then left for 20 minutes, to deprotect the dimethoxytrityl group. The solvent was distilled away, and the residue was purified by reverse phase HPLC (LC-10VP manufactured by Shimadzu Corporation, column: Merck, ~~Chromolith~~ CHROMOLITH® Performance RP-18e (4.6 × 100 mm) (a HPLC column containing a single rod of high purity monolithic silica) ; solution A: 5% acetonitrile, 0.1 M TEAA, pH 7.0; solution B: 25% acetonitrile, 0.1 M TEAA, B%: 0% → 40% (10 min, linear gradient); 60°C; 2 ml/min; 254 nm), to collect the peak of a product of interest. The solvent was distilled away under reduced pressure and the residue was dissolved in 1 ml of water (9.4 A_{260} units). In addition, the present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6214.11, measurement value: 6214.62).

Please replace the second paragraph on page 66 with the following amended paragraph:

(Example 2)

Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^p-$5C^{e2p}$-T^p-T^t (SEQ ID NO: 12)

The compound of Example 2 was synthesized in the same manner as described in Example 1 (21 A_{260} units). The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6229.12, measurement value: 6229.21).

Please replace the paragraph bridging pages 66 and 67 with the following amended paragraph:

(Example 3)

Synthesis of HO-A^p-T^p-C^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-A^p-T^p-A^p-T^p-A^p-T^p-A^p-T^p-A^p-C^p-A^p-C^p-A^p-C^p-A^p-$5C^{e2p}$-A^p-T^t (SEQ ID NO: 13)

The compound of Example 3 was synthesized in the same manner as described in Example 1 (8.9 A_{260} units). The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8530.67, measurement value: 8530.75).

Please replace the paragraph beginning on line 6 of page 67 with the following amended paragraph:

(Example 4)

Synthesis of

HO-A^p-T^p-C^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-A^p-T^p-A^p-T^p-A^p-T^p-A^p-T^p-A^p-C^p-A^p-C^p-A^p-C^p-A^p-$5C^{e2p}$-A^p-C^t (SEQ ID NO: 14)

The compound of Example 4 was synthesized in the same manner as described in Example 1 (10.1 A_{260} units). The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8515.66, measurement value: 8515.56).

Please replace the last paragraph on page 67 with the following amended paragraph:

(Reference Example 1)

$HO\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}G^{p}\text{-}G^{p}\text{-}A^{p}\text{-}G^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}T^{p}\text{-}G^{p}\text{-}A^{p}\text{-}G^{p}\text{-}G^{p}\text{-}C^{p}\text{-}T^{p}\text{-}C^{t}$ (SEQ ID NO: 1)

The compound of Reference Example 1 was synthesized by a common method using an automated nucleic acid synthesizer.

Please replace the paragraph beginning on line 5 of page 68 with the following amended paragraph:

(Reference Example 2)

$HO\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}G^{p}\text{-}G^{p}\text{-}A^{p}\text{-}G^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}T^{p}\text{-}G^{p}\text{-}A^{p}\text{-}G^{p}\text{-}G^{p}\text{-}C^{p}\text{-}T^{p}\text{-}T^{t}$ (SEQ ID NO: 2)

The compound of Reference Example 2 was synthesized by a common method using an automated nucleic acid synthesizer.

Please replace the paragraph bridging pages 68 and 69 with the following amended paragraph:

(Reference Example 3)

Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^p-C^p-T^p-C^{e2t} (SEQ ID NO: 15)

The compound of Reference Example 3 was synthesized in the same manner as described in Example 1 (0.3 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 5 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-4-N-benzoylcytidine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used and as a solid support, approximately 0.1 μmol of universal-Q 500 CPG (manufactured by Glen Research) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6200.08, measurement value: 6200.25).

Please replace the last paragraph on page 69 with the following amended paragraph:

(Reference Example 4)

Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^p-C^p-T^p-T^{e2t} (SEQ ID NO: 16)

The compound of Reference Example 4 was synthesized in the same manner as described in Example 1 (Q.94 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 9 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-5-methyluridine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used and as a solid support, approximately 0.1 μmol of universal-Q 500 CPG

(manufactured by Glen Research) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6215.09, measurement value: 6215.06).

Please replace the second paragraph on page 70 with the following amended paragraph:

(Reference Example 5)

Synthesis of HO-C^{p}-A^{p}-C^{p}-T^{p}-G^{p}-G^{p}-G^{p}-A^{p}-G^{p}-C^{p}-A^{p}-T^{p}-T^{p}-G^{p}-A^{p}-G^{p}-G^{p}-C^{p}-T^{e2p}-C^{t} (SEQ ID NO: 17)

The compound of Reference Example 5 was synthesized in the same manner as described in Example 1 (2.28 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 9 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-5-methyluridine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6200.08, measurement value: 6200.26).

Please replace the paragraph bridging pages 70 and 71 with the following amended paragraph:

(Reference Example 6)

Synthesis of HO-C^{p}-A^{p}-C^{p}-T^{p}-G^{p}-G^{p}-G^{p}-A^{p}-G^{p}-C^{p}-A^{p}-T^{p}-T^{p}-G^{p}-A^{p}-G^{p}-G^{p}-C^{p}-T^{e2p}-T^{t} (SEQ ID NO: 18)

The compound of Reference Example 6 was synthesized in the same manner as described in Example 1 (4.98 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 9 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-5-methyluridine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6215.09, measurement value: 6215.26).

Please replace the paragraph bridging pages 71 and 72 with the following amended paragraph:

(Reference Example 7)
Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^{e2p}-C^p-T^p-C^t (SEQ ID NO: 19)

The compound of Reference Example 7 was synthesized in the same manner as described in Example 1 (4.32 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 27 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-2-N-isobutyrylguanosine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6200.08, measurement value: 6199.95).

Please replace the paragraph beginning on line 8 of page 72 with the following amended paragraph:

(Reference Example 8)

Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^{e2p}-C^p-T^p-T^t (SEQ ID NO: 20)

The compound of Reference Example 8 was synthesized in the same manner as described in Example 1 (8.0 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 27 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-2-N-isobutyrylguanosine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6215.09, measurement value: 6215.06).

Please replace the paragraph beginning on line 3 of page 73 with the following amended paragraph:

(Reference Example 9)

Synthesis of HO-C^p-A^p-C^p-T^p-G^p-G^p-G^p-A^p-G^p-C^p-A^p-T^p-T^p-G^p-A^p-G^p-G^p-C^{e1p}-T^p-C^t (SEQ ID NO: 21)

The compound of Reference Example 9 was synthesized in the same manner as described in Example 1 (13.28 A_{260} units). However, as non-natural phosphoramidite, the compound (C^{e1p}), 5'-O-dimethoxytrityl-2'-O,4'-C-methylene-4-N-

benzoylcytidine-3'-O-(2-cyanoethyl N,N-diisopropyl) phosphoramidite, described in the publication, Tetrahedron (1998) 54, 3607-3630, was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6186.05, measurement value: 6186.45).

Please replace the paragraph bridging pages 73 and 74 with the following amended paragraph:

(Reference Example 10)

Synthesis of HO-C^{p}-A^{p}-C^{p}-T^{p}-G^{p}-G^{p}-G^{p}-A^{p}-G^{p}-C^{p}-A^{p}-T^{p}-T^{p}-G^{p}-A^{p}-G^{p}-G^{p}-C^{e1p}-T^{p}-T^{t} (SEQ ID NO: 22)

The compound of Reference Example 10 was synthesized in the same manner as described in Example 1 (8.0 A_{260} units). However, as non-natural phosphoramidite, the compound (C^{e1p}), 5'-O-dimethoxytrityl-2'-O,4'-C-methylene-4-N-benzoylcytidine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite, described in the publication, Tetrahedron (1998) 54, 3607-3630, was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 6201.07, measurement value: 6201.14).

Please replace the paragraph beginning on line 12 of page 74 with the following amended paragraph:

(Reference Example 11)

Synthesis of

$HO\text{-}A^p\text{-}T^p\text{-}C^p\text{-}T^p\text{-}G^p\text{-}T^p\text{-}C^p\text{-}T^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}T^t$ (SEQ ID NO: 3)

The compound of Reference Example 11 was synthesized by a common method using an automated nucleic acid synthesizer.

Please replace the paragraph beginning on line 3 of page 75 with the following amended paragraph:

(Reference Example 12)

Synthesis of

$HO\text{-}A^p\text{-}T^p\text{-}C^p\text{-}T^p\text{-}G^p\text{-}T^p\text{-}C^p\text{-}T^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^t$ (SEQ ID NO: 4)

The compound of Reference Example 12 was synthesized by a common method using an automated nucleic acid synthesizer.

Please replace the paragraph bridging pages 75 and 76 with the following amended paragraph:

(Reference Example 13)

Synthesis of

$HO\text{-}A^p\text{-}T^p\text{-}C^p\text{-}T^p\text{-}G^p\text{-}T^p\text{-}C^p\text{-}T^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}T^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}C^p\text{-}A^p\text{-}T^{e2t}$ (SEQ ID NO: 23)

The compound of Reference Example 13 was synthesized in the same manner as described in Example 1 (7.8 A_{260} units).

However, as non-natural phosphoramidite, the compound described in Example 9 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-5-methyluridine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used, and as a solid support, approximately 0.1 μmol of universal-Q 500 CPG (manufactured by Glen Research) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8516.64, measurement value: 8515.88).

Please replace the paragraph beginning on line 9 of page 77 with the following amended paragraph:

(Reference Example 14)

Synthesis of

$HO\text{-}A^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}5C^{e2t}$ (SEQ ID NO: 24)

The compound of Reference Example 14 was synthesized in the same manner as described in Example 1 (7.4 A_{260} units). However, as a solid phase carrier, approximately 0.1 μmol of universal-Q 500 CPG (manufactured by Glen Research) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8516.66, measurement value: 8516.00).

Please replace the first paragraph on page 77 with the following amended paragraph:

(Reference Example 15)

Synthesis of

$HO\text{-}A^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{e2p}\text{-}T^{t}$ (SEQ ID NO: 25)

The compound of Reference Example 15 was synthesized in the same manner as described in Example 1 (8.4 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 14 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene- 6-N-benzoyladenosine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8516.64, measurement value: 8516.32).

Please replace the paragraph bridging pages 77 and 78 with the following amended paragraph:

(Reference Example 16)

Synthesis of

$HO\text{-}A^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{e2p}\text{-}C^{t}$ (SEQ ID NO: 26)

The compound of Reference Example 16 was synthesized in the same manner as described in Example 1 (7.9 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 14 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene- 6-N-benzoyladenosine-3'-O-

(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8501.63, measurement value: 8500.70).

Please replace the last paragraph on page 78 with the following amended paragraph:

(Reference Example 17)

Synthesis of HO-A^p-T^p-C^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-A^p-T^p-A^p-T^p-A^p-T^p-A^p-T^p-A^p-C^p-A^p-C^p-A^p-C^p-A^{e2p}-C^p-A^p-T^t (SEQ ID NO: 27)

The compound of Reference Example 17 was synthesized in the same manner as described in Example 1 (9.7 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 14 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene- 6-N-benzoyladenosine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8516.64, measurement value: 8517.14).

Please replace the paragraph beginning on line 4 of page 79 with the following amended paragraph:

(Reference Example 18)

Synthesis of

$HO\text{-}A^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{e2p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{t}$ (SEQ ID NO: 28)

The compound of Reference Example 18 was synthesized in the same manner as described in Example 1 (7.2 A_{260} units). However, as non-natural phosphoramidite, the compound described in Example 14 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene- 6-N-benzoyladenosine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. The present compound was identified by negative-ion ESI mass spectrometry (calculated value: 8501.63, measurement value: 8501.65).

Please replace the paragraph bridging pages 86 to 88 with the following amended paragraph:

(Example 5) Synthesis of

$HO\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}T^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}G^{e2p}\text{-}T^{p}\text{-}G^{t}$ (SEQ ID NO: 29)

Using an automated nucleic acid synthesizer (ABI model 394 DNA/RNA synthesizer, manufactured by Perkin Elmer), the program was carried out at a scale of 40 nmol, so as to

synthesize HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^{e2p}-T^p-G^t (SEQ ID NO: 29) (hereinafter referred to as "primer A"). With regard to the concentrations of solvent, reagent and phosphoramidite in each synthesis cycle, the same concentrations as used for the synthesis of the natural oligonucleotide were applied. Approximately 0.1 μmol of CPG was used. As non-natural phosphoramidite, the compound described in Example 27 of Japanese Patent No. 3420984 (5'-O-dimethoxytrityl-2'-O,4'-C-ethylene-2-N-isobutyrylguanosine-3'-O-(2-cyanoethyl N,N-diisopropyl)phosphoramidite) was used. A protected oligonucleotide analogue having a sequence of interest was treated with concentrated ammonia water, so as to separate the oligomer from the support and so as also to remove the cyanoethyl group as protecting group on the phosphorus atom and the protecting group on the nucleobase. The solvent was distilled away under reduced pressure and the residue was purified by reverse phase HPLC (LC-10VP manufactured by Shimadzu Corporation, column: Merck, ~~Chromolith~~ CHROMOLITH® Performance RP-18e (4.6 × 100 mm) (a HPLC column containing a single rod of high purity monolithic silica), solution A: 5% acetonitrile, 0.1 M triethylamine acetate aqueous solution (TEAA), pH 7.0, solution B: acetonitrile, B%: 10% → 50% (10 min, linear gradient); 60°C; 2 ml/min; 254 nm), so as to collect the peak with the product of interest having a dimethoxytrityl group. Thereafter, water was added thereto, and the mixture was then concentrated under reduced pressure, so as to remove TEAA. Thereafter, an 80%

acetic acid aqueous solution (200 μl) was added thereto, and the mixture was then left for 20 minutes, so as to deprotect the dimethoxytrityl group. The solvent was evaporated, and the residue was purified by reverse phase HPLC (LC-10VP manufactured by Shimadzu Corporation, column: Merck, ~~Chromolith~~ CHROMOLITH® Performance RP-18e (4.6 × 100 mm) (a HPLC column containing a single rod of high purity monolithic silica), solution A: 5% acetonitrile, 0.1 M TEAA, pH 7.0, solution B: 25% acetonitrile, 0.1 M TEAA, B%: 0% → 40% (10 min, linear gradient); 60°C; 2 ml/min; 254 nm), so as to collect the peak with the product of interest. The solvent was distilled away under reduced pressure and the residue was dissolved in 1 ml of water. The present compound was identified by MALDI-TOF mass spectrometry (calculated value: 7625.0, measurement value: 7624.1).

Please replace the last paragraph on page 88 with the following amended paragraph:

(Example 6) Synthesis of $HO\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}T^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}G^{e2p}\text{-}T^{p}\text{-}A^{t}$ (SEQ ID NO: 30)

$HO\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}G^{p}\text{-}T^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}G^{p}\text{-}C^{p}\text{-}T^{p}\text{-}A^{p}\text{-}C^{p}\text{-}T^{p}\text{-}T^{p}\text{-}C^{p}\text{-}A^{p}\text{-}C^{p}\text{-}A^{p}\text{-}T^{p}\text{-}G^{e2p}\text{-}T^{p}\text{-}A^{t}$ (SEQ ID NO: 30) (hereinafter referred to as "primer B") was synthesized by the same method as that of Example 5, and the compound was then identified by MALDI-TOF mass spectrometry (calculated value: 7609.0, measurement value:

7609.2).

Please replace the second paragraph on page 89 with the following amended paragraph:

(Example 7) Synthesis of
HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^{e2p}-G^p-G^t (SEQ ID NO: 31)

HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^{e2p}-G^p-G^t (SEQ ID NO: 31) (hereinafter referred to as "primer C") was synthesized by the same method as that of Example 1 and the compound was then identified by MALDI-TOF mass spectrometry (calculated value: 7650.0, measurement value: 7649.4).

Please replace the paragraph bridging pages 89 and 90 with the following amended paragraph:

(Example 8) Synthesis of
HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^{e2p}-G^p-A^t (SEQ ID NO: 32)

HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^{e2p}-G^p-A^t (SEQ ID NO: 32) (hereinafter referred to as "primer D") was synthesized by the same method as that of Example 5, and the compound was then identified by MALDI-TOF mass spectrometry (calculated value: 7634.1, measurement value:

7634.2).

Please replace the paragraph beginning on line 6 of page 90 with the following amended paragraph:

(Reference Example 19) Synthesis of HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-T^p-G^t (SEQ ID NO: 7)

HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-T^p-G^t (SEQ ID NO: 7) (hereinafter referred to as "primer E") was synthesized by a common method using a nucleic acid automatic synthesizer. The nucleotide sequence of the present compound (primer E) is a sequence corresponding to nucleotide Nos. 60499-60523 described in GenBank accession No. AL935325.14, wherein C is converted to T at nucleotide No. 60522 and wherein A is converted to G at nucleotide No. 60523. This sequence is shown in SEQ ID NO: 7.

Please replace the paragraph bridging pages 90 and 91 with the following amended paragraph:

(Reference Example 20) Synthesis of HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-T^p-A^t (SEQ ID NO: 8)

HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-T^p-A^t (SEQ ID NO: 8) (hereinafter referred to as "primer F") was synthesized by a common method using a nucleic acid automatic synthesizer. The nucleotide sequence of the present compound (primer F) is a sequence corresponding to nucleotide Nos. 60499-60523 described in GenBank accession No. AL935325.14, wherein C is converted to T at nucleotide No. 60522. This sequence is shown in SEQ ID NO: 8.

Please replace the paragraph beginning on line 5 of page 91 with the following amended paragraph:

(Reference Example 21) Synthesis of HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-G^p-G^t (SEQ ID NO: 9)

HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-G^p-G^t (SEQ ID NO: 9) (hereinafter referred to as "primer G") was synthesized by a common method using a nucleic acid automatic synthesizer.

Please replace the paragraph bridging pages 91 and 92 with the following amended paragraph:

(Reference Example 22)

Synthesis of HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-G^p-A^t (SEQ ID NO: 10)

HO-C^p-A^p-T^p-G^p-T^p-C^p-T^p-A^p-C^p-T^p-G^p-C^p-T^p-A^p-C^p-T^p-T^p-C^p-A^p-C^p-A^p-T^p-G^p-G^p-A^t (SEQ ID NO: 10) (hereinafter referred to as "primer H") was synthesized by a common method using a nucleic acid automatic synthesizer.